

REMARKS

Claims 1-6, 11, 12, 14, 19, 20, 32-51, 54-56, 58, and 59 are currently pending. Claims 32-40 are cancelled by the present amendment. Claims 44-51, 54-56, 58, and 59 are withdrawn from consideration at this time. Claims 1-6, 11, 12, 14, 19, 20, and 41-43 are rejected. Claims 1, 11, and 12 are amended. New claims 63-71 are added. Support for new claims 63-65 is found in claim 4. Support for new claims 66-68 is found in paragraph [0091] on page 39 of the application as filed. Support for new claims 69-71 is found in paragraph [0015] on page 4 of the application as filed. The amendments to claims 11 and 12 merely seek correct typographical errors or avoid ambiguity with regard to substituent groups.

No new matter has been added. These amendments are made without prejudice and without intent to abandon any originally claimed subject matter. Applicant reserves the right to pursue this subject matter in an application claiming priority to the present application.

Interview

Applicant thanks the Examiner for granting a telephonic interview on December 7, 2009. The state of the art at the time of filing, the cited art, and possible amendments to the claims were discussed and progress was made. Specifically, Inventor M. Papisov explained to the Examiner how one of ordinary skill could not have predicted at the time the present application was filed that polyacetals or polyketals would be able to form the claimed conjugates due to their unpredictable reactivity and stability.

Applicant and Examiner also discussed that the monomeric substrates taught by Cervigni and Rose are dissimilar to the polymeric substrates used to prepare the claimed conjugates and how one of ordinary skill would cannot assume that reaction conditions for monomeric substrates will apply to polymeric substrates. Applicant further explained how the polymeric carrier is susceptible to hydrolytic degradation under acidic conditions, and an amendment to the claims was discussed in this context. Applicant has amended claim 1 to include the language "the molecular weight of the carrier is between about 0.5 and about 1500 kDa." Support for this amendment is found in paragraph [0091] on page 39 of the application as filed. Claim 1 has also been amended to incorporate language from claims 11 and 12.

Applicant submits herewith a Declaration under 37 CFR § 1.132 to reiterate and expand on these points. The rejections levied in the Office Action are discussed below.

Rejection of claims 1-12, 14, 19-22, and 41-43 under 35 U.S.C § 103(a).

Claims 1-12, 14, 19-22, and 41-43 were previously rejected under 35 U.S.C § 103(a) as unpatentable over Cervigni *et al.*, in view of U.S. Patent No. 5,958,398 by Papisov (“the ‘398 patent”), U.S. Patent No. 5,612,037 by Huebner (“the ‘037 patent”), and G. Hermanson, Preparation of Liposome Conjugates and Derivatives, Bioconjugate Techniques, pp. 552-589, (“Hermanson”), and the Examiner has maintained this rejection.

In the previous Response, Applicant argued that one of ordinary skill would not have a reasonable expectation of success to form the claimed conjugates when combining the method of Cervigni with the polyacetals of the ‘398 patent. Specifically, Applicant pointed out that the harsh conditions exemplified by Cervigni (*i.e.*, pH 3 for 120 hours) would cause nearly complete hydrolysis of the PHF main chain. The Examiner now asserts that “this harsh condition is not the only pH condition taught by the Cervigni methods” and quotes from Cervigni “an oxime bond is formed regioselectively under mild aqueous conditions in a one-pot reaction.” Applicant respectfully disagrees. The mere use of the word “mild” by the author to describe this ligation condition does not render the exemplified condition less acidic, nor does it constitute a different ligation condition other than pH 3. Regardless of the author’s characterization of the method (*i.e.*, “harsh” vs. “mild”), Applicant respectfully submits that the only ligation condition exemplified by Cervigni is pH 3 for either 120 hours or an undisclosed time (see 2nd paragraph of Experimental Procedure on page 1231 and caption of Scheme 2 on page 1230). That the author apparently considers these conditions to be “mild” does not change the fact that they would completely hydrolyze the PHF main chain.

The Examiner argues that Cervigni cites Rose *et al.*, wherein an oxime formation is carried out at pH 4.6 at 22 °C. Applicant respectfully submits that, as described in the attached Declaration under 37 CFR § 1.132, the state of the art at the time the instant application was filed indicated—at best—a significant level of unpredictability regarding the reactivity and stability of

polyacetals. Therefore, it would not have been obvious to one of ordinary skill in the art to combine the Cervigni or Rose oxime-forming conditions with the polyacetals of the '398 patent. Rather, the skilled artisan would assume the harsh pH conditions taught by these references could in fact depolymerize the polyacetal main chain.

Moreover, as explained in the interview on December 7, 2009 and discussed in the Declaration, even if it could be believed that a polyacetal could survive such harsh pH conditions, one of ordinary skill would not necessarily have a reasonable expectation of success with polymeric substrates when applying reaction conditions that have been demonstrated on monomeric substrates. Thus, the skilled practitioner would not have had a reasonable expectation of success to form the claimed conjugates when combining the methods of Cervigni or Rose with the polyacetals of the '398 patent. Applicant respectfully requests that the rejection be removed.

In addition, Applicant respectfully submits that the oxidation of polysaccharides to generate polyaldehydes and the transformation of aldehydes to oximes have both been known for decades. Yet, as described in the Declaration under 37 CFR § 1.132, prior to Applicant's filing of the instant application, no published reports exemplified the formation of the instantly claimed conjugates in an enabling manner. The closest description is the inventor's own paper, Papisov MI. *ACS Symposium Series*, Vol. 786, **2001**, pp. 301-314 (attached herewith as **Exhibit C**), which proposes the possibility of such conjugates. As explained in the Declaration, however, Applicant respectfully submits that a person having ordinary skill in the art, reading the Papisov 2001 article, would not be led to produce the instantly claimed conjugates.

Applicant invites the Examiner to call the undersigned at (617) 248-5175 with any questions pertaining to the above-identified application in order to expedite prosecution of this case.

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Respectfully submitted,

____/Brenda Herschbach Jarrell/_____

Brenda Herschbach Jarrell, PhD, JD
Reg. No. 39,223

PATENT GROUP
CHOATE, HALL & STEWART
Two International Place
Boston, MA 02110
Tel: (617) 248-5175
Fax: (617) 502-5002
patentdocket@choate.com